Medicines & Healthcare products Regulatory Agency

MHRA

The Onward Journey of Your Data

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EBF 12th Open Symposium

21 November 2019



UK Pre-Election Period


www
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In Our Own Little Bubble?

"We don't deal with clinical patients. We only receive and analyse samples"

(GCC Survey 2015 – GCP Clinical Sample Bioanalysis)

Analytical Reports

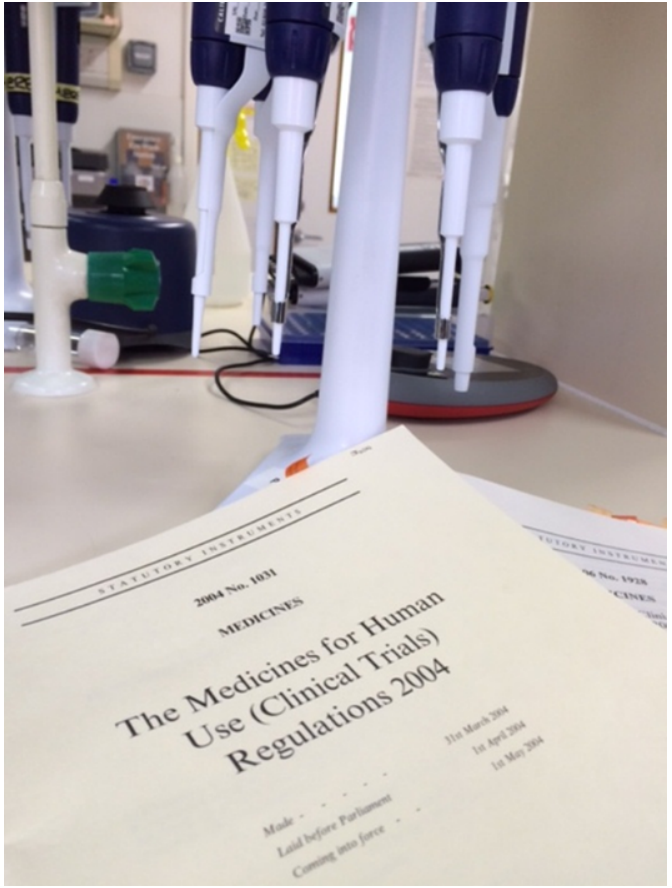
"Sponsors should focus on trial activities essential to ensuring human subject protection and the reliability of trial results.

Quality management includes the design of efficient clinical trial protocols and tools and procedures for data collection and processing, as well as the collection of information that is essential to decision making".

ICH E6R2

Data Release

- History of academic collaboration
- Exchange of trial results outside of standard practice
- No quality checks
- Status of data unclear
- Data submitted by sponsor for licence extension
- Significant differences between datasets



Dose Escalation

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 July 2017
EMEA/CHMP/SWP/28367/07 Rev. 1
Committee for Medicinal Products for Human Use (CHMP)

Guideline on strategies to identify and mitigate risks for first-in-human and early clinical trials with investigational medicinal products

Adopted by CHMP for release for consultation	10 November 2016
Start of public consultation	15 November 2016
End of consultation (deadline for comments)	28 February 2017
Adopted by CHMP	20 July 2017
Date of coming into effect	01 February 2018

Keywords	First-in-human, phase I, early clinical trials, investigational medicinal product, risk mitigation, integrated protocols, multiple ascending dose, dose escalation.

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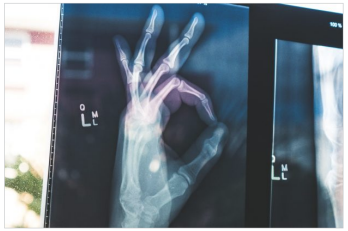
Dose Escalation - is it GCP compliant?

Jennifer Martin, 26 November 2018 - Compliance matters, Good clinical practice



So, this is my first ever blog post (both work and personal) and I wanted to use this to talk about differing dose escalation (DE) practices, especially between first in human (FIH) healthy volunteer trials and those in patients (FIP). In reality, if you are complying with Good Clinical Practice (GCP) they should be the same.

More frequently, with the advancement of medicine, FIH trials are being conducted in patients. Biologicals, cell therapy or oncology medicines may be too toxic or not suitable to give to healthy volunteers, so patients become the first humans to receive these medicines.

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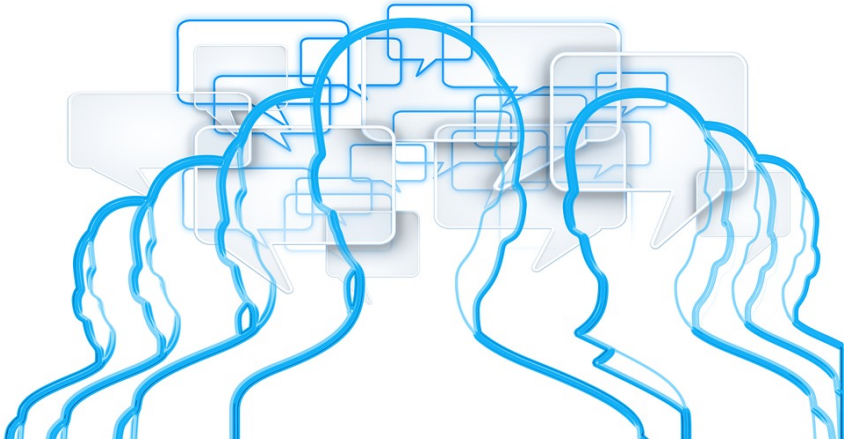
Flawed Decision Making?

- Data released by lab including data from failed runs or where data was incomplete
- Data from lab provided to the PK / stats but re-reported for decision making

Further Investigation

- Trigger for sponsor / phase I unit inspections
- Review of information used for decision making
- Poor flow of information
- Lack of supporting documentation
- Lack of transparency



Fit For Purpose Report

- Report containing necessary and relevant information
- Understand what data is to be used for
- Time for analysis, reporting and quality checks
- Patient safety is paramount!

EUROPEAN MEDICINES AGENCY
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1 December 2016
EMA/CHMP/ICH/135/1995
Committee for Human Medicinal Products

Guideline for good clinical practice E6(R2)
Step 5

Adopted by CHMP for release for consultation	23 July 2015
Start of public consultation	4 August 2015
End of consultation (deadline for comments)	3 February 2016
Final adoption by CHMP	15 December 2016
Date for coming into effect	14 June 2017

the intended use of the system and the potential of the system to affect human subject protection and reliability of trial results.

2. The principles of ICH GCP

2.1.

Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirement(s).

2.2.

Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.

2.3.

The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society.

2.4.

The available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial.

2.5.

Clinical trials should be scientifically sound, and described in a clear, detailed protocol.

2.6.

A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/independent ethics committee (IEC) approval/favourable opinion.

2.7.

The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist.

2.8.

Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective task(s).

2.9.

Freely given informed consent should be obtained from every subject prior to clinical trial participation.

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2.10.

All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification.

ADDENDUM

This principle applies to all records referenced in this guideline, irrespective of the type of media used.

2.11.

The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).

2.12.

Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP). They should be used in accordance with the approved protocol.

2.13.

Systems with procedures that assure the quality of every aspect of the trial should be implemented.

ADDENDUM

Aspects of the trial that are essential to ensure human subject protection and reliability of trial results should be the focus of such systems.

3. Institutional Review Board / Independent Ethics Committee (IRB/IEC)

3.1. Responsibilities

3.1.1.

An IRB/IEC should safeguard the rights, safety, and well-being of all trial subjects. Special attention should be paid to trials that may include vulnerable subjects.

3.1.2.

The IRB/IEC should obtain the following documents:

- trial protocol(s)/amendment(s), written informed consent form(s) and consent form updates that the investigator proposes for use in the trial, subject recruitment procedures (e.g. advertisements), written information to be provided to subjects, Investigator's Brochure (IB), available safety information, information about payments and compensation available to subjects, the investigator's current curriculum vitae and/or other documentation evidencing qualifications, and any other documents that the IRB/IEC may need to fulfil its responsibilities.
- The IRB/IEC should review a proposed clinical trial within a reasonable time and document its views in writing, clearly identifying the trial, the documents reviewed and the dates for the following:

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Any Questions?

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